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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,557	07/22/2002	Gerald Juergen Roth	5/1271PCT	3607

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EXAMINER	
WRIGHT, SONYA N	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,557	ROTH ET AL.	
	Examiner	Art Unit	
	Sonya Wright	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-20 and 23-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-20 and 23-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *0304* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's amendment filed December 18, 2003. Claims 13-20 and 23-29 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-20, 23, and 25-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CaAFC, 1988)):

1) Nature of invention.

2) State of prior art.

3) Level of ordinary skill in the art.

4) Level of predictability in the art.

5) Amount of direction and guidance provided by the inventor.

6) Existence of working examples.

7) Breadth of claims.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

1) Nature of the invention.

Claim 13-20 is drawn to a compound of the formula (I) wherein any carboxy, amino or imino group present is optionally substituted by a group which can be cleaved in vivo, or the physiologically acceptable salts and isomers thereof. Claims 23 and 25-29 are drawn to methods of use, such as a method of treating haemangiomas, metastasisation, rheumatoid arthritis, psoriasis, a method of inhibiting tumour cell proliferation, etc. . . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

2) State of the prior art.

The prior arts do not indicate which group(s) which can be cleaved in vivo, or which "isomers" are useful in the instant invention. The prior arts do not indicate that the instant compound is useful in treating all forms of the diseases claimed in claims 23 and 25-29.

3) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. There are a vast number of, forms of haemangiomas, metastasisation, rheumatoid arthritis, psoriasis, etc. . ., and applicant does not give support for "treating" all forms of these disorders. There are a vast number of isomers of the claimed compound, and Applicant does not show how to make isomers of the claimed compound. Further, Applicant does not support that all isomers are useful as claimed.

Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of formula (1) for treating all forms of the diseases claimed.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

4) Level of predictability in the art.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Hence, in the absence of a showing of treating all forms of the diseases claimed by the compound of formula (1), one of skill in the art is unable to fully predict possible results from the administration of the compound of formula (1) due to the unpredictability of the art pertaining to the diseases claimed.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The various forms of these disorders have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. The art pertaining to isomers remains highly unpredictable. Different isomers may have different properties and different methods of use.

5) Amount of direction and guidance provided by the inventor.

In terms of guidance, Applicant describes the compound of formula I having pharmacological properties on p. 1, lines 6-18, and p. 31, lines 16-32 and pages 32-35 in their entirety. However, the limited guidance on p. 1, lines 6-18, and p. 31, lines 16-32 and pages 32-35 in their entirety lacks sufficient enablement for the scope of the method of use claims. Also, Applicant does not show how to make an isomer of the instant compound.

Applicant describes "a group which can be cleaved in vivo" on p. 9, lines 16-27 and page 10, lines 1-10. However, the limited description on page 9, lines 16-27 and page 10, lines 1-10 does not embrace the full scope of the claims regarding "a group which can be cleaved in vivo".

The guidance is limited because various forms of diseases claimed have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol.

6) Existence of working examples.

Applicant provides compound Examples 1-306 on pages 36-105. Applicant provides Examples 12-18 on compositions and suppositories, on pages 106-109. However, the limited examples do not support the full scope of diseases claimed. Applicant provides no examples of isomers of the instant compound.

7) Breadth of claims.

The claims are extremely broad due to the various forms of diseases, isomers, and the various "groups which can be cleaved in vivo". Applicant has not shown support that the instant compound can be used to treat all forms of the diseases claimed. Applicant has not shown support that all isomers and all "groups which can be cleaved in vivo" are useful in the instant claims.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not use the claimed invention without undue experimentation.

In view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage

in undue experimentation to test how the instant compound is useful in treating all forms of the diseases claimed, with no assurance of success.

It is suggested that Applicant limit the method claims to diseases which are supported in the specification by biological data. It is suggested that Applicant limit the isomers in the claims to isomers which are supported in the specification. It is suggested that Applicant limit the "group which can be cleaved in vivo" to the groups which are supported in the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is drawn to a process for preparing a compound of the formula (I) which comprises converting a compound of the formula (I) in the manner described on page 18.

It is unclear whether the compounds that formula (I) is converted to are supported in the genus of claim 13. Clarification is requested because compounds and processes of preparing compounds which are outside of the genus of claim 13 have not been searched.

Response to Arguments

Applicant's amendment has overcome the objection to claims for containing non-elected subject matter. Applicant's arguments filed December 8, 2003 have been fully

considered but they are not persuasive with respect to the rejection of method claims under 112 first paragraph.

Applicant identifies where support for inhibiting tumour cell proliferation and solid tumours can be found the specification. Applicants indicate that the declaration of Ulrike Tontsch-Grunt presents objective evidence for demonstrating activity against solid tumours for the compounds of the present invention. Applicants argue that the declaration states that the activity for inhibiting tumour diseases is commensurate in scope for the claimed subject matter. Applicants indicate where support for a method of inhibiting endothelial cell proliferation in the specification and where data demonstrating the activity is found in a table.

However, the disorders related to tumour cell proliferation and solid tumours embrace a plethora of diseases. Applicants specification and the declaration do not support that the instant compound can treat all forms of disorders related to tumour cell proliferation and solid tumours. Therefore, the specification does not enable the full scope of the claims.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Hence, in the absence of a showing of treating all forms of the diseases claimed by the compound of formula (1), one of skill in the art is unable to fully predict possible results from the

administration of the compound of formula (1) due to the unpredictability of the art pertaining to the diseases claimed.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The various forms of these disorders have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. Therefore, the method claims are rejected under 35 U.S.C. 112 first paragraph (supra).

Applicant's arguments with respect to the objection to the specification for missing a reference to the continuing data have been found persuasive and the objection has been withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sonya Wright, whose telephone number is (703) 308-4539. The examiner can normally be reached on Monday-Friday from 8:00 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (703) 308-4537. The Unofficial

fax phone number for this Group is (703) 308-7922. The Official fax phone numbers for this Group are (703) 308-4556 or 305-3592.

When filing a FAX in Technology Center 1600, please indicate in the Header (upper right) "Official" for papers that are to be entered into the file, and "Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [joseph.mckane@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-1235.

Kamal Saeed
for Joseph K. McKane
Supervisory Patent Examiner
Group 1600

Sonya Wright

March 12, 2004